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EXAMINER

RAE, CHARLESWORTH E

ART UNIT PAPER NUMBER

1614

NOTIFICATION DATE DELIVERY MODE

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ELECTRONIC

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

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|                              |                               |                              |  |
|------------------------------|-------------------------------|------------------------------|--|
| <b>Office Action Summary</b> | Application No.<br>10/583,135 | Applicant(s)<br>WEILL ET AL. |  |
|                              | Examiner<br>Charleswort Rae   | Art Unit<br>1614             |  |

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

### Status

- 1) ☒ Responsive to communication(s) filed on 16 June 2006.
- 2a) ☐ This action is FINAL.                      2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

### Disposition of Claims

- 4) ☒ Claim(s) 1-6 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-6 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

### Application Papers

- 9) ☒ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 16 June 2006 is/are: a) ☐ accepted or b) ☒ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

### Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All    b) ☐ Some \*    c) ☐ None of:
1. ☒ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

### Attachment(s)

- |   |   |
|---|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)   | 4) <input type="checkbox"/> Interview Summary (PTO-413)<br>Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)                                  | 5) <input type="checkbox"/> Notice of Informal Patent Application                       |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)<br>Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____  |

Applicant's application and accompanying preliminary amendment, filed 6/16/06, is acknowledged.

### **Status of the Claims**

Claims 1-6 are currently pending in this application and are the subject of the Office action.

### **Priority**

Receipt of a non-English certified copy of the foreign priority application, received 6/16/06, is acknowledged and made of record.

### **Objection to the Specification/Drawings**

The specification is objected to for failing to provide a Brief Description of Drawings in accordance with MPEP 608.01(f). For instance, no reasonable description of Figure 9 is provided to enable someone of skill in the art to interpret the data disclosed in said figure. In addition, the figures are difficult to interpret e.g. see Figure 35.

In addition, the use of the trademark "taxol" has been noted in this application (e.g. page 12, line 22). It should be capitalized wherever it appears and be accompanied by the generic terminology. Although the use of trademarks is permissible in patent applications, the proprietary nature of the marks should be respected and every effort made to prevent their use in any manner which might adversely affect their validity as trademarks. Thus, applicant may correct the above noted deficiency by simply replacing the brand name "taxol" with the generic name.

Correction of this deficiency is requested.

### **Objection to the Claims**

Claim 1 recites the terms "leukocyte-protecting" and "antitumor-and-leukocyte ." The use of the "-" to separate the terms is objected.

Claims 4 and 5 are objected to for reciting the term "taxol." The term "Taxol" should be capitalized wherever it appears and be accompanied by the generic terminology. Although the use of trademarks is permissible in patent applications, the proprietary nature of the marks should be respected and every effort made to prevent their use in any manner which might adversely affect their validity as trademarks. Thus, applicant may correct the above noted deficiency by simply replacing the brand name "taxol" with the generic name.

### **Claim rejections – 35 USC 103(a)**

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was

not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-6 are rejected under 35 U.S.C. 103(a) as being unpatentable over Bianco (US Patent Application Publication No. 2004/0047835), in view of Huang et al. (US Patent Publication No. 2002/0106348), and further in view of Rocklage et al. (US Patent 4,978,763).

For purposes of this rejection, the term "*an antitumor and leukocyte-protecting active ingredient and an antitumor-and-leukocyte-protecting amount of a superoxide dismutase and glutathione reductase mimetic*" is construed to mean an antitumor active ingredient, and a leukocyte-protecting active ingredient possessing superoxide dismutase and glutathione reductase mimetic activities, wherein the leukocyte-protecting active ingredient is present in a leukocyte protecting amount.

Bianco (US Patent Application Publication No. 2004/0047835) teach combinations of drug conjugates with other therapeutic agents, including chemotherapy drugs, wherein said combinations are used for the treatment of diseases associated with cell proliferation such as tumors; the therapeutic agents may be conjugated to a polymer, or, derivatized with a chelating agent such as DTPA, DOTA, TETA, DMSA, DTTP, and DPDP (abstract; and paras 0003 to 0050). DPDP is reasonably construed to satisfy the term "*leukocyte-protecting active ingredient,*" as recited in claim 1. The term "leukocyte protecting amount" as recited in claim 1 is reasonably construed to be within the skill and knowledge of an artisan skilled in the art with routine experimentation e.g.

clinical laboratory blood analyses are routinely performed to determine the level of leukocytes in the blood. Although Bianco does not exemplify Mn-DPDP conjugates, Bianco teaches that embodiments in which the paclitaxel or another drug is conjugated to a water soluble metal chelator, the composition may further comprise a chelated metal ion e.g. an ionic form of manganese (page 6, para 0051). The use of Mn-DPDP (also referred to as mangafodipir; see also the National Library of Medicine – Medical Subject Headings, 2007 MeSH) is reasonably envisaged by teaching of chelated ionic form of manganese in view of the express teaching of DPDP as being a preferred water soluble chelator. (para 0050). Claims 2 and 6 recite the term mangafodipir. Claim 6 recites the term *“said mimetic is used in combination with an antitumor agent capable of inducing a reactive oxygen species production in cells.”* Bianco teaches that chemotherapy drugs that may be used in combination with a drug conjugated to a polymer or chelator include, doxorubicin, etoposide, mitomycin, fluorouracil, irinotecan, gemcitabine, 5-FU, oxaliplatin, paclitaxel, cisplatin, carboplatin, belomycin, amifostine, vincristine, and streptozocin (para 0092 and 0097). Instant claim 1 recites the term *“anticancer medicinal product”* and the term *“an antitumor ... active ingredient;”* claim 4 recites the terms *“doxorubicin, mitomycin C, etoposide, platinum derivatives, 5-fluorouracil, irinotecan, gemcitabine, streptozocin, bleomycin and vincristine; claim 5 recites the terms “oxaliplatin, 5-fluorouracil and taxol,”* which clearly overlaps with the teaching of Bianco. Bianco teaches that in certain embodiments, conjugation or derivatization of the drug causes the drug to be more water soluble, more readily taken up by a cell or tissue, or less toxic (page 3, para 0021, lines 2-9). For example, Bianco teaches that

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conjugated paclitaxels improve the efficacy of paclitaxel-based anti-cancer therapy by providing water-soluble and controlled-release paclitaxel-derived compositions (para 0019). However, Bianco does not specifically teach the instantly claimed “anticancer medicinal product comprising *“an antitumor and leukocyte-protecting active ingredient and an antitumor-and-leukocyte-protecting amount of a superoxide dismutase and glutathione reductase mimetic” in combination with a “superoxide dismutase and glutathione reductase mimetic, wherein the antitumor agent is capable of inducing a reactive oxygen species production in cells.”*

Huang et al. (US Patent Publication No. 2002/0106348) teach that a variety of chemical compounds and physical modalities are known to increase the intracellular concentration of reactive oxygen, including cisplatin, bleomycin, retinoic acid derivatives, anthracyclines (e.g. doxorubicin, daunorubicin), hyperthermia, ultraviolet rays, X-rays or  $\gamma$ -rays (page 1, para 0011). Claim 3 recites the term “an antitumor agent capable of inducing a reactive oxygen species production in cells.” Huang et al. specifically teach therapeutic methods wherein a compound or compounds that inhibits SOD activity is administered in combination with an agent or agents that increases intracellular reactive oxygen intermediate accumulation and methods for enhancing the antineoplastic/tumoricidal properties of an SOD inhibitor by concomitantly increasing intracellular oxygen radical concentrations with the administration of an additional agent that increases reactive oxygen intermediates within the target cancer cell.

Rocklage et al. (US Patent 4,978,763) teach that manganese chelates are particularly useful as MRI contrast agents because manganese being normally present

in the body in low concentrations, and because Mn(II) has optimum properties for enhancing MRI contrast; manganese chelates, including MnDPDP are disclosed (col. 1, line 17 to col. 2, line 32). Claims 2, and 6 recite the term "*mangafodipir*."

Based on the teaching of Rocklage et al. of the superiority of manganese chelates, someone of skill in the art would have been motivated to combine the teachings of the above cited prior art references to create the instant claimed inventive concept.

Thus, someone of skill in the art at the time the instant invention was made would have found it obvious to create the instant invention with reasonable predictability.

#### **Relevant Art of Record**

The below cited art references made of record and relied upon are considered pertinent to applicant's invention.

Federle et al. teach that a method of detecting liver disease comprising the injection of mangafodipir trisodium (MnDPDP) in a dose of 5  $\mu$ mol/kg IV to patients with focal liver disease (Federle et al. Efficacy and safety of mangafodipir trisodium (MnDPDP) injection for hepatic MRI in adults: results of the U.S. multicenter phase III clinical trials – Efficacy of early imaging. Journal of Magnetic Resonance Imaging. 2000;12:689-701; see especially abstract; and page 699, col. 2).

Capizzi et al. (US Patent 5,846,958) teach methods of stimulating the growth of hematopoietic progenitor cells, wherein thiols and related compounds are used in stimulating the growth of hematopoietic progenitor cells in vitro and in vivo, and methods of using said compounds for the treatment of marrow failure states and immunodeficient conditions, including but not limited to myelodysplastic syndromes and

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acquired immunodeficiency syndrome (abstract). Capizzie et al. teach that growth factors such as GM-CSF, M-CSF, and G-CSF can be used, for example, to lessen the need for blood transfusions, speeding bone marrow recovery following transplantation and cytotoxic cancer therapy, but cytokines are both difficult and costly to produce (col. 1, line 60 to col. 2, lines 52). Capizzi et al. teach WR 151327 is a thiophosphate reducing agent with oxygen-free radical scavenging capacity, which may be directly administered to patients for the treatment of any conditions that manifest reduced numbers of circulating blood cells, including leucopenia, at doses of 100 to 740 mg/m<sup>2</sup> (col. 1, line 60 to col. 4, line 29).

Stankiewicz et al. teach that cyclophosphamide is an inactive cytostatic, which is metabolized into active metabolites mainly in the liver; reactive oxygen species (ROS) are formed during the bioactivation, which can modify the components of both healthy and neoplastic cells leading to decreased antioxidative capacity (Stankiewicz et al. Effects of amifostine on liver oxidative stress caused by cyclophosphamide administration to rats. Drug Metabol Drug Interact. 2002;19(2):67-82, abstract only). Stankiewicz et al. teach that co-administration of cyclophosphamide and amifostine nearly prevented changes in activities of superoxide dismutase, glutathione reductase and catalase; intraperitoneal administration of cyclophosphamide was found to decrease the activity of liver antioxidative enzymes i.e. superoxide dismutase, glutathione peroxidase, and glutathione reductase.

#### **Claim rejections – 35 USC 112 – Second Paragraph**

The following is a quotation of the second paragraph of 35 USC 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-6 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 recites the confusing language "*an antitumor and leukocyte-protecting active ingredient and an antitumor-and-elukocyte-protecting amount of a superoxide dismutase and glutathione reductase mimetic.*" This language renders the claim indefinite because it is not clear if the term refers to a single active agent (i.e. having *superoxide dismutasemimetic and glutathione reductase mimetic activity*), or multiple active ingredients (i.e. an antitumor active ingredient and an leukocyte protecting active ingredient or, an antitumor active ingredient and an leukocyte protecting active ingredient and a glutathione reductase mimetic). Also, the terms "leukocyte-protecting" "anttitumor-and-leukocyte" and

Claims 2-6 are rejected for the same reason as these claims fail to correct the deficiency of the independent claim from which they depend.

#### **Claim Rejections – 35 USC 112 – First Paragraph**

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-6 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while enabling for certain anticancer medicinal product/composition comprising, for example, oxaliplatinol and mangafodipir, does not reasonably provide enablement for synergistic combinations comprising any and all antitumor compounds in combination with any and all leukocyte protecting active ingredients. This is a scope of enablement rejection.

To be enabling, the specification of the patent application must teach those skilled in the art how to make and use the full scope of the claimed invention without undue experimentation. *In re Wright*, 999 F.2d 1557, 1561 (Fd. Cir. 1993). Explaining what is meant by "undue experimentation," the Federal Circuit has stated that:

The test is not merely quantitative, since a considerable amount of experimentation is permissible, if its is merely routine, or if the specification in question provides a reasonable amount of guidance with respect to the direction in which experimentation should proceed to enable the determination of how to practice a desired embodiment of the claimed invention. *PPG v Guardian*, 75 F.3d 1558, 1564 (Fed. Cir. 1996).

The factors that may be considered in determining whether a disclosure would require undue experimentation are set forth in *In re Wands*, 8 USPQ2d 1400 (CAFC 1988) at 1404 wherein, citing *Ex parte Forman* 230 USPQ 546 (BdApls 1986) at 547 the court cited eight factors:

- 1) the quantity of experimentation necessary,
- 2) the amount of direction or guidance provided,
- 3) the presence or absence of working examples,

- 4) the nature of the invention,
- 5) the state of the prior art,
- 6) the relative skill of those in the art,
- 7) the predictability of the art, and
- 8) the breadth of the claims

These factors are always applied against the background understanding that scope of enablement varies inversely with the degree of unpredictability involved. *In re Fisher*, 57 CCPA 1099, 1108, 427 F.2d 833, 839, 166 USPQ 18, 24 (1970). Keeping that in mind, the Wands factors are relevant to the instant fact situation for the following reasons:

1. The nature of the invention, state and predictability of the art, and relative skill of those in the art.

The invention in general relates to a medicinal product/composition comprising an antitumor active ingredient and a superoxide dismutase/glutathione reductase mimetic agent method for treating arteriosclerosis comprising administering to a subject in need thereof an effective amount of a compound of the formula recited in claim 21.

The relative skill of those in the art is high, generally that of an M.D. or Ph.D. It is noted that the chemical and medical arts are generally unpredictable, requiring each embodiment to be individually assessed for chemical, pharmacologic, pharmaceutical, and clinical efficacy. The more unpredictable an area, the more specific enablement is

necessary in order to satisfy the statute. (see *In re Fisher*, 427 F.2d 833, 166 USPQ 18 (CCPA 1970)).

Applicant asserts that singular properties of mangafodipir, as compared with other antioxidants, in particular other SOD mimetics tested, appear to be linked to its double activity of superoxide dismutase mimetic and glutathione reductase mimetic ((page 7, first full para.). Applicant also discloses other SOD mimetics that possess a glutathione reductase mimetic activity, such as dipyridoxal phosphate derivatives in the form of divalent cation chelates (e.g. copper chelates, zinc chelates or, advantageously, manganese chelates (page 7, lines 17-24). Applicant discloses examples of antitumor agents capable of inducing, in cells, ROS production, including antitumor agents (page 8, lines 1-13). Applicant asserts that because of the simultaneous nature of their cytotoxic and cytostatic effect with respect to tumor cells, and their protective effect with respect to normal leukocytes, the superoxide dismutase and glutathione reductase mimetics make it possible to significantly increase the therapeutic index of the anticancer medicinal products with which they are combined (page 8, lines 15-25).

Huang et al. (US Patent Publication No. 2002/0106348) teach that a variety of chemical compounds and physical modalities are known to increase the intracellular concentration of reactive oxygen, including cisplatin, bleomycin, retinoic acid derivatives, anthracyclines (e.g. doxorubicin, daunorubicin), hyperthermia, ultraviolet rays, X-rays or  $\gamma$ -rays (page 1, para 0011; see also page 4, para 0089 to page 6, para 0107)). Huang et al. specifically teach therapeutic methods wherein a compound or compounds that inhibits SOD activity is administered in combination with an agent or

agents that increases intracellular reactive oxygen intermediate accumulation and methods for enhancing the antineoplastic/tumoricidal properties of an SOD inhibitor by concomitantly increasing intracellular oxygen radical concentrations with the administration of an additional agent that increases reactive oxygen intermediates within the target cancer cell. Huang et al. teach that anti-cancer agents include biological agents (biotherapy), chemotherapy agents, and radiotherapy agents, and are generally provide in a combined amount to kill or inhibit proliferation of the cell (page 7, para 0121, last 5 lines; and para. 0123). However, although a number of SOD inhibitors have been identified, the majority are either highly toxic or otherwise unsuitable for administration in a therapeutic regimen (page 3, para 0078, lines 1-4).

Martin et al. teach administration of mangadipir trisodium via injection to patients to image focal liver abnormalities (Martin et al. Sequential use of gadolinium chelate and mangadipir trisodium for the assessment of focal liver lesions: initial observations. Magn Reson Imaging. October, 2000;18(8)955-963; abstract only).

Dai et al. (Dai et al. A potential synergistic anticancer effect of paclitaxel and amifostine on endometrial cancer. Cancer Res. October, 2005; 65(20):9517-24; abstract only) teach that the two-drug regimen of paclitaxel and amifostine inhibited s.c. tumor growth as well as improved mouse survival significantly more than paclitaxel alone. Dai et al. teach that a potential anticancer synergy exists between amifostine and paclitaxel in vitro and in vivo, while amifostine maintained a protective role in peripheral blood profiles. Dai et al. disclose that the dual specificity of amifostine action should be further investigated. Also, Dai et al. disclose that even though paclitaxel is one of the most

effective chemotherapeutic agents, its usefulness is still limited in advanced and recurrent endometrial cancer.

Neuwelt et al. (US Patent 7,022,315) teach that thiol-based chemoprotectant agent, including N-acetylcysteine (NAC), and sodium thiosulfate (STS), markedly protects against injury from diagnostic or therapeutic intra-arterial procedures and disclose methods for treating or mitigating the side effects of cytotoxic cancer therapy for tumors located in the head or neck and brain tumors (abstract). Neuwelt et al. exemplify chemotherapy agents (e.g. cisplatin, carboplatin, melphalan, and etoposide) in combination with NAC, or STS (see Fig 5 and fig 6; col. 1, line 24 to col. 2, line 6; and col. 4, line 66 to col. 5, line 25). Neuwelt et al. also teach thiol amifostine (also known as Ethiol or WR2721). See col. 2, lines 48-65.

2. The breadth of the claims

The instant claims are relatively broad in scope. For example, claim 1 recites the term "anticancer medicinal product" which reasonably encompass the treatment of any and all cancers in any and all mammalian species. Claim 1 also recites the term "antitumor and leukocyte-protecting active ingredient and an antitumor-and-leukocyte-protecting amount of a superoxide dismutase and glutathione reductase mimetic," given its broadest reasonable possible interpretation, this term is construed to encompass any and all antitumor active ingredients, including gene therapy, immunotherapy, chemotherapy, radiation therapy, any leukocyte protecting agent with or without antitumor activity that possess superoxide dismutase and glutathione reductase mimetic effects, and combinations of said therapies. Claim 3 recites the term

*“an antitumor agent capable of inducing a reactive oxygen species production in cells,”* which given its broadest reasonable possible interpretation encompasses any cell, including targeted cancer cell and non-targeted normal host cells. Because the contemplated anticancer effect to be achieved would necessarily vary depending upon the pharmaceutical/pharmacologic properties of the specific antitumor active agent and leukocyte protecting active agent, and relative compatibilities, the level of predictably in practicing the claimed invention would be greatly diminished.

3. The amount of direction or guidance provided and the presence or absence of working examples

Applicant discloses results of studies conducted in C57BL/6 mice, following the injection of Hepa 1-6 cells, wherein the injection of SOD mimetics such as MnTBAP, CuDIPS or mangafodipir decreased the tumor volume by 42%, 9%, and 34%, respectively (page 20-22, Example 7); the coadministration of MnTBAP and CuDIPDS with oxaliplatin does not significantly increase antitumor effect of oxaliplatin, but administration of MnDPDP to mice treated with oxaliplatin decreased the tumor volume by 63% at one month, compared with the animals treated only with oxaliplatin (page 22, lines 16-34). However, no specific guidance is disclosed on how use the genus of antitumor and leukocyte protecting active ingredients for treating non-liver cancers. Based on the instant disclosure, the applicant at best has provided specific direction or guidance only for a medicinal product comprising MnDPDP to mice treated with oxaliplatin. No reasonably specific guidance is provided for an artisan skilled in the art to extrapolate

the disclosed in vitro and in vivo data (see Figures 1- 35) to treat any cancer cell type without conducting extensive experimentation.

4. The quantity of experimentation necessary

In view of the uncertainty and unpredictability of the art as evidenced by the discussion of the prior art, it is reasonable to surmise that this level of uncertainty in the art would require one skilled in the art to conduct more than routine experimentation in order to practice the claimed invention commensurate with the scope of the claims.

For the reasons stated above, claims 21-30 are rejected under 35 USC 112, first paragraph, for lack of scope enablement because the specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with the claims.

**LACK OF WRITTEN DESCRIPTION UNDER 35 U.S.C. § 112, FIRST PARAGRAPH:**

Claims 1-6 are rejected under 35 U.S.C. § 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The specification discloses chemicals which meet the written description and enablement provisions of 35 USC 112, first paragraph. However, claims 1-6 are directed to encompass compounds which only correspond in some undefined way to specifically instantly disclosed chemicals, as evidenced by the recitation of functional terms such as "antitumor" active agent, "leukocyte-protecting " and "a superoxide

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dismutase and glutathione reductase mimetic." None of the undisclosed functionally described compounds meet the written description provision of 35 USC § 112, first paragraph, due to lacking chemical structural information for what they are and chemical structures are highly variant and encompass a myriad of possibilities. The specification provides insufficient written description to support the genus encompassed by the claim.

Vas-Cath Inc. v. Mahurkar, 19 USPQ2d 1111, makes clear that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of *the invention*. The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed*." (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See Vas-Cath at page 1116.)

With the exception of the above specifically disclosed chemical structures, the skilled artisan cannot envision the detailed chemical structure of the encompassed compounds, analogs, etc., regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it. The chemical structure itself is required. See Fiers v. Revel, 25 USPQ2d 1601, 1606 (CAFC 1993) and Amgen Inc. V. Chugai Pharmaceutical Co. Ltd., 18 USPQ2d 1016. In Fiddes v. Baird, 30 USPQ2d 1481, 1483, claims directed to mammalian FGF's were found unpatentable due to lack of written description for the broad class. The specification provided only the bovine sequence. Finally, University of California v. Eli Lilly and Co., 43 USPQ2d 1398, 1404, 1405 held that:

...To fulfill the written description requirement, a patent specification must describe an invention and do so in sufficient detail that one skilled in the art can clearly conclude that "the inventor invented the claimed invention." Lockwood v. American Airlines, Inc., 107 F.3d 1565, 1572, 41 USPQ2d 1961, 1966 (1997); In re Gosteli, 872 F.2d 1008, 1012, 10 USPQ2d 1614, 1618 (Fed. Cir. 1989) (" [T]he description must clearly allow persons of ordinary skill in the art to recognize that [the inventor] invented what is claimed."). Thus, an applicant complies with the written description requirement "by describing the invention, with all its claimed limitations, not that which makes it obvious," and by using "such descriptive means as words, structures, figures, diagrams, formulas, etc., that set forth the claimed invention." Lockwood, 107 F.3d at 1572, 41 USPQ2d at 1966.

Therefore, only the disclosed chemically structurally defined chemicals, but not the full breadth of the claim(s) meet the written description provision of 35 USC § 112, first paragraph. The species specifically disclosed are not representative of the genus because the genus is highly variant. Applicant is reminded that Vas-Cath makes clear that the written description provision of 35 USC § 112 is severable from its enablement provision. (See page 1115.)

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Charlesworth Rae whose telephone number is 571-272-6029. The examiner can normally be reached between 9 a.m. to 5:30 p.m. Monday to Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ardin Marschel, can be reached at 571-272-0718. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR.

Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have any questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 800-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the

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automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-

1000.

8 November 2007

CER

BRIAN-YONG S. KWON  
PRIMARY EXAMINER

A handwritten signature in black ink, appearing to read 'B. Kwon', with a long horizontal stroke extending to the right.